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Diet and Stomach Cancer Risk in Warsaw, Poland

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Abstract: *Some of the world's highest rates of stomach cancer are found in Poland. Reasons for the increased incidence are not known, but high intake of sausages and other preserved foods and low intake of fresh fruits and vegetables may be involved. A case-control study comprising residents newly diagnosed with stomach cancer during 1994–96 and controls randomly selected from the general population was conducted in Warsaw, Poland. Standardized interviews were conducted to ascertain usual consumption of 118 common foods and beverages and other exposures. Using data from direct interviews with 274 cases and 463 controls, odds ratios of stomach cancer were calculated as estimates of risks associated with dietary factors, adjusting for age, sex, education, smoking, and caloric intake.*

Risk of stomach cancer was inversely related to intake of total fruits and dark green-yellow vegetables and to indices of vitamins C and E and α- and β-carotenes. However, risk was not significantly increased among those with high intake of pickled/salted vegetables and sausages. Risks were positively associated with increased intake of breads/cereals/rice/pasta and other refined grains, as well as a high carbohydrate index. Our findings add to the evidence of a protective effect of fruits and certain vegetables on stomach cancer risk, but do not indicate that high intake of sausage and other preserved foods typical in the Polish diet has contributed to the country's elevated stomach cancer incidence. Our data also suggest that high carbohydrate consumption may influence risk, but further confirmation is needed.

Introduction

Gastric cancer remains the second most common cancer in incidence and mortality worldwide, despite its overall decline (1). Poland has one of the world's highest incidence rates of stomach cancer, with age-standardized incidence rates of 23.0 in males and 8.0 in females per 100,000 in the year 2000 (2). Lifestyle factors, especially dietary factors, are thought to be important in modifying the risk of stomach cancer. However, the only consistent finding in relation to diet is an inverse association with intake of raw fruits and, to a lesser extent, vegetables. Associations with other dietary factors, including a diet high in meat, grains and starchy foods, allium compounds, and salt, are inconclusive (3).

Among the nutrients, dietary intake of vitamin C and β-carotene have been consistently associated with a reduction in stomach cancer risk. Other components of fruits and vegetables (e.g., folate, dietary fiber, and other carotenoids) have been investigated in a few recent studies with mixed results (4–10).

In Poland, the typical diet before 1990 included relatively high intakes of total calories, preserved meat, and preserved vegetables, and low intakes of fresh fruits and vegetables. The availability of fruits and vegetables was restricted seasonally and limited in variety (11). It was hypothesized that such traditional dietary practices might have contributed to the high incidence rates of stomach cancer in Poland. To test this hypothesis, we conducted a population-based case-control study in Warsaw, Poland.

Material and Methods

The study design has been described in detail previously (12). In brief, cases consisted of Warsaw residents newly diagnosed with stomach cancer between March 1, 1994, and April 30, 1996, who were identified by collaborating physicians in each of the 22 hospitals serving the entire study area of Warsaw. Slides and tissue blocks were sought from each case for uniform review and classification according to the system of Lauren (13). In addition, the Cancer Registry files were reviewed regularly to ensure completeness of case as-

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certainment. Controls were randomly selected from among Warsaw residents using a computerized registry of all legal residents of Poland. They were frequency-matched to cases by sex and age in five-year strata.

Of 515 eligible cases identified, interviews were conducted in person for 324 cases (62.9%) and with next of kin (mainly spouses) for 140 cases (27.2%). A 30-ml blood sample was collected from 304 cases. Of the 549 controls identified, 480 (87.4%) agreed to be interviewed and 433 (78.9%) agreed to donate a 30-ml blood sample. Detailed information on lifetime tobacco use, alcohol consumption, family history of cancer, childhood living conditions, lifetime occupation, and usual diet prior to 1990 was obtained.

Diet was assessed using a food frequency questionnaire (FFQ), which was a modification of the Block questionnaire (14). Usual frequency of intake prior to 1990 (a year of political and economic changes in Poland resulting in significant increases in food selection and availability) was assessed for 118 food and beverage items. Dietary questionnaires were processed using the National Cancer Institute-Block analysis program (DietSys, Version 3.70, National Cancer Institute, Bethesda, MD; 15). The FFQs were edited according to standard criteria to identify and remove individuals who skipped more than 15% of questionnaire items or who consumed more than 30 different food items per day. Using these criteria, we excluded an additional 50 cases and 17 controls from the current analyses. Chi-square tests were used to compare distributions of demographic variables, smoking status, and tumor characteristics between cases included and excluded from the analysis, as well as between controls and cases included in the analysis.

Intake of individual food items and food groups was categorized into quartiles defined by weekly frequency of consumption among controls. Intake for each food group was obtained by summing the frequency of consumption for individual food items in the group. Appendix A shows food grouping and Appendix B shows the cutpoints for all food groups.

Nutrient content of each food item was estimated using both U.S. (16) and Polish (17) food tables. For several unique Polish complex dishes, original recipes were used to calculate food components and nutrients (18). The Polish Food Composition Tables were not used as a main source for nutrients because a number of dietary constituents of interest (e.g., carotenoids) were not included and access to documentation and sampling information for the Tables was limited.

In the nutrient analysis, gender-specific portion sizes for every food item were obtained from the Pol-MONICA database, comprised of 24-hour dietary recalls. The study was conducted in Warsaw in 1988 and included 1,397 participants (19). For food items that were not available in the Pol-MONICA data set, DietSys portion sizes were adopted. Portion sizes estimated from Pol-MONICA study and those from DietSys were compared and did not show major differences.

The measure of association between stomach cancer risk and food or nutrient intake was the odds ratio (OR). The lowest quartile of intake for each food group or nutrient was used as the referent. To account for potential confounding by nondietary factors, adjusted OR estimates and corresponding 95% confidence intervals (CI) were obtained by applying multivariate logistic regression analyses. All the regression models included terms for age, sex, education level, cigarette smoking, and caloric intake. For calorie adjustment in the analyses of nutrients, density variables were created (Appendix C). The nutrient density variable (intake/1,000 kcal) represents the effect of increasing the percentage of nutrient intake while keeping total energy intake constant (20). The quartile cutpoints for nutrient density variables were based on distribution among controls. Further adjustment for alcohol intake or *Helicobacter pylori* infection (as determined by serum antibody titers) did not materially alter risk estimates and thus were not included in the final models.

To assess the quality of data obtained by proxy, we conducted a reliability study on a subsample of the 324 directly interviewed cases. The next of kin of 112 directly interviewed cases were asked the same questions about the case three to six months later. The reliability of self-reported versus proxy-reported FFQs was examined by overall percentage of agreement, sensitivity, and (κ statistics (21) and showed unsatisfactory agreement (κ = 0.05–0.37). Therefore, except where otherwise indicated, we excluded all 140 cases with proxy interviews.

Results

Compared with cases included in the analysis, excluded cases (including proxy cases and cases with questionable diet data) tended to be older and less educated, but were comparable in gender and smoking distributions (Table 1). Excluded cases also were more likely to have tumors with advanced or unknown stages at diagnosis and unknown Lauren classification, but similar in tumor localization to the cases included in the analysis. The included cases and controls were similar in distribution by age and gender, but cases were more likely to be heavy smokers and slightly less educated (Table 1).

Food Groups

Table 2 presents ORs according to quartiles of frequency consumption for 19 food groups. Risks declined significantly with increasing consumption of total fruits, particularly when juices were included [*P* (for trend) = 0.005], with a 47% reduction in risk in the highest quartile of intake. Consumption of various fresh vegetables tended to be inversely related to risk, but a statistically significant trend was seen only for dark green-dark yellow vegetables [*P* (for trend) = 0.002]. This result remained after additional adjustment for fruit intake, suggesting an independent effect. The moderate inverse associations with high intake of tubers and allium vegetables were not statistically significant. No association was found for cruciferous vegetables or pickled/salted vegetables.

Risk of stomach cancer increased with increasing consumption of total grains, with a nearly twofold excess (OR = 1.9) in the highest quartile of intake. The excess risk was largely confined to the groups of bread/cereal/rice/pasta [*P* (for trend) < 0.001] and refined grains [P (for trend) = 0.02]. Consumption of fresh fish was inversely related to risk [*P* (for

Table 1. Distribution of Controls, Cases Included in Dietary Analysis, and Cases Excluded According to Demographic Characteristics and Adjustment Variables

Variable	Controls n = 463 (%)	Cases Included n = 274 (%)	Cases Excluded n = 190 (%)	P Value
Gender				
Male	304 (65.7)	175 (63.9)	127 (66.8)	
Female	159 (34.3)	99 (36.1)	63 (33.2)	
Controls vs. cases included				0.622
Cases incl. vs. cases excluded				0.509
Age				
<50	57 (12.3)	37 (13.5)	18 (9.5)	
50–59	79 (17.1)	48 (17.5)	25 (13.2)	
60–69	182 (39.3)	110 (40.2)	67 (35.3)	
70+	145 (31.3)	79 (28.8)	80 (42.1)	
Controls vs. cases included				0.899
Cases incl. vs. cases excluded				0.025
Education				
≤high school	170 (36.7)	119 (43.4)	87 (45.8)	
some college	161 (34.8)	96 (35.0)	73 (38.4)	
≥college graduate	132 (28.5)	59 (21.5)	30 (15.8)	
Controls vs. cases included				0.074
Cases incl. vs. cases excluded				0.298
Smoking (pack-yrs)				
Nonsmoker	180 (38.9)	81 (29.6)	57 (30.0)	
<10	46 (9.9)	25 (9.1)	17 (8.9)	
10–20	44 (9.5)	22 (8.0)	18 (9.5)	
20–29	62 (13.4)	35 (12.8)	22 (11.6)	
30–39	62 (13.4)	42 (15.3)	20 (10.5)	
40–49	30 (6.5)	33 (12.0)	17 (8.9)	
50+	36 (7.8)	35 (12.8)	32 (16.8)	
Unknown	3 (0.6)	1 (0.4)	7 (3.7)	
Controls vs. cases included				0.023
Cases incl. vs. cases excluded				0.107
Localization				
Cardia only		31 (11.3)	30 (15.8)	
Distal stomach		204 (74.5)	130 (68.4)	
Cardia/distal		29 (10.6)	23 (12.1)	
Unknown		10 (3.6)	7 (3.7)	
Cases incl. vs. cases excluded				0.473
Lauren classification				
Intestinal		189 (69.0)	121 (63.7)	
Diffuse		46 (16.8)	20 (10.5)	
Indeterminate		25 (9.1)	19 (10.0)	
Unknown		14 (5.1)	32 (16.8)	
Cases incl. vs. cases excluded				0.0003
Staging				
Localized		55 (20.1)	13 (6.8)	
Regional metastasis		84 (30.7)	33 (17.4)	
Distant metastasis		70 (25.5)	74 (38.9)	
Unknown		65 (23.7)	70 (36.8)	
Cases incl. vs. cases excluded				<0.0003

trend) = 0.13], with about a 40% reduction in the highest quartile of intake. Poultry was not widely consumed and was not related to risk. Consumption of other animal products, including red meat, smoked meat/fish, and sausages, tended to be positively related to risk, but none of the associations reached statistical significance. Risks in the highest quartile of intake of red meat, smoked meat/fish, and sausages were 1.5, 1.3, and 1.2, respectively. We did not find an association with consumption of fried/broiled meat versus baked/roasted/stewed meats. However, when well-browned meat was consumed, risk was significantly increased (OR = 1.7; 95% CI = 1.21–2.27) compared with those who never or almost never consumed well-browned meat (data not shown). No association was seen for dairy products or sweets. Simultaneous adjustments for dark green-yellow vegetables did not affect the associations for grains and meat groups.

Nutrients

Summary statistics of nutrient and caloric intake by case-control status for men and women separately are presented in Table 3. Risk of stomach cancer showed a positive

Table 2. Odds Ratios (OR) with 95% Confidence Intervals (CI) for Stomach Cancer According to Consumption Level of Food Groups[a]

	Quartiles of Weekly Frequency Consumption				
Food Group	1 (low)	2	3	4 (high)	*P* (for trend)
Fruits (including juices)	1.00	1.04 (0.70–1.55)	0.76 (0.50–1.17)	0.53 (0.33–0.86)	0.005
Fruits (excluding juices)	1.00	1.36 (0.90–2.06)	0.75 (0.52–1.09)	0.57 (0.32–1.05)	0.02
Vegetables, total	1.00	1.01 (0.66–1.53)	0.77 (0.50–1.20)	0.83 (0.52–1.33)	0.22
Cruciferous vegetables	1.00	1.08 (0.71–1.65)	0.98 (0.64–1.48)	0.92 (0.56–1.50)	0.59
Dark green-dark yellow vegetables	1.00	0.93 (0.61–1.41)	0.61 (0.40–0.93)	0.56 (0.35–0.89)	0.002
Tubers, roots	1.00	1.00 (0.67–1.47)	0.73 (0.46–1.16)	0.78 (0.50–1.22)	0.13
Allium vegetables	1.00	1.06 (0.70–1.60)	0.92 (0.60–1.40)	0.78 (0.50–1.22)	0.20
Raw vegetables	1.00	0.66 (0.42–1.03)	0.75 (0.51–1.13)	0.81 (0.52–1.26)	0.26
Pickled/salted vegetables	1.00	1.11 (0.74–1.67)	1.36 (0.87–2.11)	0.98 (0.61–1.56)	0.81
Grains, total	1.00	1.37 (0.71–1.57)	1.58 (0.49–1.15)	1.89 (1.00–2.85)	0.02
Bread, cereals, rice, pasta	1.00	1.47 (0.91–2.38)	1.67 (0.97–2.86)	2.40 (1.35–4.25)	<0.001
Refined grains	1.00	1.50 (0.94–2.39)	1.70 (1.03–2.81)	1.80 (1.04–3.13)	0.02
Whole grains	1.00	1.01 (0.65–1.57)	1.32 (0.86–1.04)	1.05 (0.65–1.69)	0.37
Dairy products	1.00	0.96 (0.63–1.46)	0.87 (0.54–1.40)	0.94 (0.57–1.54)	0.67
Meat, poultry, and fish	1.00	1.20 (0.77–1.88)	0.99 (0.61–1.61)	1.40 (0.84–2.35)	0.55
Poultry	1.00	0.89 (0.61–1.31)			
Fish	1.00	0.88 (0.61–1.24)	0.72 (0.45–1.16)	0.62 (0.37–1.02)	0.13
Red meat	1.00	1.24 (0.79–1.95)	1.19 (0.73–1.92)	1.51 (0.90–2.51)	0.28
Smoked meat/fish	1.00	1.32 (0.88–1.97)	1.35 (0.83–2.18)	1.30 (0.86–1.96)	0.31
Sausages	1.00	1.13 (0.74–1.71)	0.75 (0.48–1.17)	1.23 (0.79–1.93)	0.81
Sweets	1.00	1.05 (0.69–1.61)	1.00 (0.64–1.57)	0.89 (0.56–1.42)	0.53

a: All estimates were adjusted for age, sex, education, smoking, and calories from food.

Table 3. Daily Intakes of Macronutrients, Selected Micronutrients, and Energy[a]

	Males			Females		
Nutrient	Cases	Controls	2-Tailed *P* Value	Cases	Controls	2-Tailed *P* Value
Calorie (kcal)	3,100.8 ± 795.4	3,102.1 ± 768.5	0.986	2,378.6 ± 690.8	2,323.4 ± 602.0	0.500
Protein (g)	117.1 ± 33.1	117.4 ± 30.3	0.919	90.8 ± 26.3	89.2 ± 24.8	0.631
Carbohydrates (g)	375.0 ± 100.7	368.3 ± 101.7	0.486	294.6 ± 89.4	286.0 ± 81.6	0.429
Fat total (g)	127.5 ± 36.2	130.6 ± 34.7	0.368	94.8 ± 29.8	93.3 ± 25.4	0.652
Saturated fat (g)	47.3 ± 14.5	48.7 ± 13.7	0.307	35.7 ± 11.1	35.1 ± 9.5	0.646
Linoleic acid (g)	15.8 ± 6.1	16.7 ± 5.9	0.137	12.7 ± 5.5	12.6 ± 4.7	0.921
Oleic acid (g)	46.9 ± 14.2	48.1 ± 13.6	0.366	34.4 ± 11.9	33.6 ± 9.9	0.557
Cholesterol (mg)	518.1 ± 168.1	524.3 ± 170.7	0.700	383.0 ± 124.6	385.3 ± 125.7	0.885
Salt from food (g)	6,786.8 ± 1,546.4	6,805.9 ± 1,653.5	0.901	4,936.5 ± 1,280.5	4,848.0 ± 1,172.0	0.570
Fiber total (g)	20.6 ± 5.7	21.1 ± 5.8	0.351	17.1 ± 5.2	17.0 ± 5.2	0.911
Fiber from fruit/veg. (g)	8.6 ± 3.4	9.6 ± 3.7	0.005	7.5 ± 3.2	8.0 ± 3.3	0.214
Fiber from beans (g)	2.1 ± 2.1	2.5 ± 2.0	0.013	1.3 ± 1.1	1.5 ± 1.3	0.162
Vitamin C (mg)	78.0 ± 29.6	84.4 ± 36.7	0.051	74.4 ± 43.3	72.0 ± 33.9	0.609
Folate (µg)	334.7 ± 88.8	331.5 ± 87.7	0.707	281.0 ± 86.7	270.6 ± 83.6	0.341
Vitamin E (a-te)	7.5 ± 3.2	8.1 ± 3.1	0.047	6.6 ± 2.7	6.5. ± 2.5	0.869
Total vitamin A (RE)	2,525.2 ± 1,154.0	2,717.3 ± 1,220.3	0.091	2,253.8 ± 1,053.5	2,275.8 ± 1,000.2	0.867
Retinol (µg)	29.4 ± 29.8	37.8 ± 32.7	0.006	12.2 ± 16.8	15.9 ± 16.2	0.078
α-carotene (µg)	563.9 ± 420.8	706.5 ± 502.4	0.002	684.5 ± 516.5	683.5 ± 423.7	0.986
β-carotene (µg)	1,966.9 ± 1,194.6	2,384.2 ± 1,446.2	0.001	2,304.3 ± 1,416.9	2,327.8 ± 1,330.0	0.895
Lycopene (µg)	2,604.0 ± 1,906.4	2,693.8 ± 2,817.1	0.708	1,784.6 ± 1,254.0	1,893.6 ± 1,735.2	0.588
Lutein (µg)	977.5 ± 595.3	1,125.5 ± 747.0	0.025	1,205.2 ± 768.1	1,234.4 ± 975.8	0.801
Cryptoxanthin (µg)	4.8 ± 5.4	5.4 ± 6.5	0.306	9.9 ± 15.9	8.1 ± 11.1	0.277

a: Values are means ± SD.

Table 4. Odds Ratios (OR) with 95% Confidence Intervals (CI) for Stomach Cancer According to Consumption of Specific Nutrients[a]

	Quartiles of Consumption (Intake/1,000 kcal)				
Nutrient or Other Dietary Constituent	1 (low)	2	3	4 (high)	*P* (for trend)
Calorie[b] (kcal)	1.00	0.85 (0.56–1.31)	0.85 (0.56–1.31)	0.91 (0.60–1.40)	0.70
Protein (g)	1.00	0.86 (0.56–1.33)	1.04 (0.68–1.59)	0.91 (0.59–1.40)	0.83
Carbohydrates (g)	1.00	1.01 (0.64–1.60)	1.50 (0.96–2.33)	1.39 (0.89–2.18)	0.04
Fat, total (g)	1.00	1.09 (0.73–1.63)	0.59 (0.37–0.93)	0.81 (0.52–1.25)	0.01
Saturated fat (g)	1.00	1.11 (0.74–1.64)	0.69 (0.44–1.07)	0.77 (0.49–1.21)	0.06
Linoleic acid (g)	1.00	0.58 (0.39–0.87)	0.59 (0.39–0.90)	0.50 (0.32–0.78)	<0.01
Oleic acid (g)	1.00	0.81 (0.54–1.21)	0.56 (0.36–0.87)	0.63 (0.40–0.97)	<0.01
Cholesterol (μg)	1.00	1.08 (0.71–1.64)	0.94 (0.61–1.43)	0.90 (0.58–1.38)	0.45
Salt from foods (g)	1.00	0.91 (0.60–1.41)	0.77 (0.49–1.21)	0.95 (0.60–1.49)	0.71
Fiber, total (g)	1.00	0.89 (0.59–1.34)	1.07 (0.69–1.63)	0.73 (0.46–1.17)	0.40
Fiber from fruits/vegetables (g)	1.00	0.64 (0.41–0.98)	0.85 (0.55–1.30)	0.49 (0.30–0.82)	0.03
Fiber from beans (g)	1.00	0.61 (0.39–0.94)	0.46 (0.30–0.70)	0.50 (0.32–0.78)	<0.01
Vitamin C (mg)	1.00	0.96 (0.66–1.40)	0.80 (0.50–1.26)	0.68 (0.42–1.11)	0.17
Folate (μg)	1.00	1.01 (0.65–1.57)	1.20 (0.77–1.85)	1.26 (0.81–1.98)	0.17
Vitamin E (a-te)	1.00	0.91 (0.60–1.36)	0.71 (0.47–1.08)	0.60 (0.38–0.94)	0.002
Total vitamin A (RE)	1.00	0.67 (0.44–1.02)	0.72 (0.47–1.10)	0.67 (0.44–1.04)	0.12
Retinol (μg)	1.00	0.61 (0.40–0.93)	0.54 (0.35–0.82)	0.41 (0.26–0.65)	<0.0001
Carotenoids (μg)					
α-carotene	1.00	0.85 (0.57–1.29)	0.58 (0.37–0.91)	0.55 (0.35–0.86)	0.003
β-carotene	1.00	0.84 (0.56–1.28)	0.93 (0.61–1.43)	0.51 (0.32–0.82)	0.01
Lycopene	1.00	1.18 (0.77–1.84)	1.02 (0.66–1.59)	1.19 (0.77–1.82)	0.60
Lutein	1.00	1.31 (0.86–2.00)	1.05 (0.67–1.65)	0.97 (0.61–1.56)	0.63
Cryptoxanthin	1.00	1.10 (0.72–1.68)	0.79 (0.51–1.23)	1.06 (0.68–1.65)	0.79

a: All estimates were adjusted for age, sex, education, smoking, and calories from foods.
b: Calorie is not a density variable, and sex-specific quartiles for calories are based on controls.

association with intake of carbohydrates [*P* (for trend) = 0.04] and inverse association with intake of total fats [*P* (for trend) =0.01] (Table 4). The inverse association was more pronounced for unsaturated fats (linoleic acid and oleic acid) than for saturated fats. No clear trend was found with increased intake of total calories, protein, cholesterol, or salt from foods (sodium). Although the relationship with total fiber was weak, significant inverse associations were observed for fiber from fruits and vegetables ($P = 0.03$) and beans ($P < 0.01$), with a 50% reduction in risks at the highest quartiles of intake. When both fruits/vegetables and fiber from fruits/vegetables were included in the model, an effect of fiber remained. The same was true for beans and fiber from beans. A number of antioxidant vitamins were associated with reduced risks of stomach cancer, including vitamin C, vitamin E, and total vitamin A and retinol, but only vitamin E and retinol showed statistically significant trends ($P = 0.002$). Among the carotenoids (other constituents of vitamin A, mostly from plant sources), significant inverse associations were found only for α-carotene [*P* (for trend) = 0.003] and β-carotene [*P* (for trend) = 0.01], but not for lycopene, lutein, or cryptoxanthin. Folate intake was not significantly related to risk, but the trend tended to be positive.

Further adjustment for fruits, dark green-yellow vegetables, or "bread, cereals, rice, and pasta" did not substantially alter the risk estimates for nutrients. Separate analyses restricted to cases with an intestinal type of tumor yielded results for food groups and nutrients similar to those for all cases combined (data not shown).

The Pearson correlation coefficients between intake of total fruit and the main fruit constituents, including ascorbic acid, α-carotene, and β-carotene were $r = 0.38$, $r = 0.32$, and $r = 0.33$, respectively. To investigate the extent to which protective effects from intake of total fruits were attributable to their content of ascorbic acid and carotenoids, these nutrients were added to a multivariate model. The ORs for total fruit intake remained significant, suggesting that some other active substances in fruits may lower the risk of stomach cancer or that estimates of micronutrient levels were measured with error. Similar analyses for dark green-yellow vegetables was possible only for vitamin C [α- and β-carotene was too highly correlated with dark green-yellow vegetables ($r = 0.80$ and $r = 0.81$, respectively)], and the ORs were essentially unchanged.

Discussion

With few exceptions (22–24), fresh fruits and vegetables have been consistently linked to a reduced risk of stomach cancer in a variety of studies in different populations (3). In our study, however, the protective effect of vegetables was mainly confined to consumption of dark green-yellow vegetables. Allium vegetables have been studied in many countries with diverse consumption patterns. They have been hypothesized to protect against stomach cancer by inhibiting the bacterial conversion of nitrate to nitrite in the stomach and by their antibiotic properties against *H. pylori*. The protective role of allium vegetables reported in some studies (25–28) was not strongly supported by our data, although we did find a nonsignificant inverse trend in risk. Onions are the most commonly used allium vegetable in Poland, yet findings for onions are less consistent than for garlic. Also, the content of possible preventive compounds may vary depending on whether they are consumed raw or cooked. In Poland, they are mostly consumed as cooked condiments and, as such, are highly correlated with the intake of red meat.

It was also hypothesized (29–30) that refrigeration use may lead to decreased risk of stomach cancer indirectly, via increased intake of fresh vegetables and fruits and reduced intake of preserved foods. In these studies, reduced risk of stomach cancer (RR = 0.5) was observed after long-term use of refrigeration (29 years). In Poland, the refrigerator became commonly available in 1970–75, and a low intake of fruits and vegetables before 1989 was mainly due to low availability and narrow selection of fruits and vegetables on the market, not from the lack of refrigeration itself. In our data, there was no association with refrigeration use.

The previous literature regarding cereals (grains) is abundant but inconsistent and suggestive of increased risk with higher consumption of cereals (3). A positive association with starchy foods or carbohydrates was reported in several studies of stomach cancer (31–35), but not in all (36). A protective effect of whole-grain cereals was suggested in a few case-control studies (28,34,37). Our data do not support a protective effect of whole-grain cereals, but the consumption of whole-grain foods is low in Poland. On the other hand, total consumption of grains and bread/cereal/rice/pasta was a risk factor in our study, but this finding was attributable to diet rich in refined grains. We found inverse associations with intake of fiber from fruits and vegetables and fiber from beans, but not with total dietary fiber. Previous case-control studies have shown inverse associations with total dietary fiber intake and stomach cancer risk (35,38,39). One explanation may be that Polish diets that are rich in carbohydrates and low in dietary fiber (rich in refined cereals and low in whole-grain cereals) are also relatively low in protective micronutrients. Another possible mechanism proposed for colon cancer by Giovannucci (40) is that a diet rich in refined grains and carbohydrates elicits high plasma levels of insulin, which might promote tumor development through an increase in activity of insulin-like growth factor (IGF)-I and IGF-II.

Salt intake has been linked to stomach cancer risk in a large number of studies (25,26,41–43). Plausible biological mechanisms have been proposed by Correa (44) to suggest a role for salt in gastric carcinogenesis. We found no association between the intake of salt from foods and stomach cancer risk. Because the main foods in Poland that are of high salt content, such as sausages, pickled foods, and bread, are universally consumed, it was difficult to detect any differences. In addition, data were not available on table salt use in our study. One previous study from Poland has shown a significant increase in risk of stomach cancer for above-average consumption of table salt (29).

Our study, like many others (37,45,46), found only a modest and nonsignificant increase in risk with red meat intake and a nonsignificant decrease in risk with fish intake, indicating no evidence that meat itself is related to the risk of stomach cancer. Others have found an association with well-done or fried meat (47–49). We also found a significantly elevated risk with consumption of well-browned, fried/broiled/baked/roasted red meat, consistent with the hypothesis that pyrolysis carcinogens, such as heterocyclic amines that are formed during high-temperature cooking of meat, may play a role in gastric carcinogenesis.

Sausages, which are widely consumed in Poland, were investigated in this study because of their high content of sodium, nitrosamines, and nitrite. Evidence relating to diets high in smoked foods is conflicting. Correa et al. (50) found a positive association with smoked foods among blacks but not among whites in the United States. Nonsignificant reduction in risk was found in Belgium (34) and Sweden (38). Our study does not add much to these hypotheses. This may be due to the fact that sausages are the most universally consumed food item in Poland. We found only a modest, nonsignificant increase in risk of stomach cancer with the intake of smoked foods. The lack of association between sausage intake and stomach cancer risk in our study contradicts findings in a previous hospital-based case-control study in Poland that showed a significant increase in intestinal type of stomach cancer risk for the highest levels of consumption of sausages (51). Other studies also reported a small, often nonsignificant, elevation in risk at the highest consumption of various cured meats (ham, bacon, sausage; 24,34,52).

Antioxidants can neutralize DNA-damaging free radicals, such as those generated by smoking, and therefore may lower the risk of gastric cancer (53–55). In addition to their antioxidative effects, Vitamins C and E, retinol, and carotenoids may reduce stomach cancer risk through other mechanisms (56). Vitamins C and E may inhibit in vivo formation of potentially carcinogenic N-nitroso- compounds (57). Retinol converted from carotenoids plays an important role in the regulation of cell differentiation and may prevent malignant cell transformation (58). Previous studies have shown a relatively consistent protective effect of dietary intake of vitamin C (33,37,45,59). However, results on the effect of retinol and vitamin A intake are not consistent. The interpretation of previous results on vitamin A is complicated by the diversity of vitamin A sources (natural preformed vitamin A is found in animal foods). The vitamin A and carotenoid data previously available in food composition tables only allowed the intake of total vitamin A activity to be estimated. Information about the intake of specific carotenoids or retinoids has only recently been made available in some food composition tables. Thus, previous epidemiologic interpretations of the role of carotenoids assumed that the active factor in fruits and vegetables was β-carotene and was related to its potential for vitamin A activity. In fact, many fruits and vegetables are poor sources of β-carotene but good sources of other carotenoids that have little or no vitamin A activity. Green and yellow vegetables contain no preformed vitamin A, but different carotenoids (only some of them can be metabolized to form retinol, the physiologically active vitamin A). Dark green vegetables contain predominantly lutein, tomatoes are rich in lycopene, and carrots are the major source of β-carotene (60).

In our study, α- and β-carotenes seem to explain a large part of the apparent effect of dark green-yellow vegetables, whereas vitamin C explains only a small part of the association observed for fruits. Carotenes were found to be protective of stomach cancer in a number of case-control studies (8,9,31,32,37,42,59,61). However, a prospective study (7) reported positive associations with β-carotene and retinol, but no association with α-carotene, lutein, lycopene, and cryptoxanthin. Our study supports the hypothesis that the decrease in risk of stomach cancer may be attributable to high dietary intake of α- and β-carotene and retinol, but not lycopene, lutein, and cryptoxanthin, which are known to have no vitamin A activity (62). The lack of association for the latter carotenoids in our study might be explained, in part, by low intake and the relatively short season for consumption of tomatoes, kale, and collard greens in Poland, the main sources for lycopene and lutein.

Limitations

A potential limitation of this study is the high percentage of proxy interviews that were excluded from the analyses. Because the main reason for proxy interviews was the death of the patient, there is a possibility of survival bias. If the identified risk factors also decrease survival after stomach cancer diagnosis, then exclusion of deceased patients may result in underestimation of the true risks for these factors. If the risk factors are associated with increased survival, then exclusion of deceased patients may lead to overestimation of the true risks for these factors. Likewise, our study results may not be fully generalizable to cases with advanced cancer because proxy interviews were conducted for the majority of these cases.

We tried to use information from the proxy data to see if estimates of ORs would be changed or their precision increased. As described in Appendix D, the basic assumption underlying this analysis is that the direct measurement is the gold standard and that, given the direct measurement, the proxy provides no additional information on risk of disease. The analysis implicitly uses proxy data to estimate the missing direct measurement. If the correlation between direct and proxy measurements is poor, this analysis implicitly gives less weight to cases with proxy data than to cases with direct data. Unreported analyses show that use of proxy data yielded negligible changes in ORs or in the precision of the estimates for the 13 nutrients and micronutrients we examined. For example, we estimated an OR for consumption of saturated fat for men and women combined as 1.35 with standard error 0.19 for direct data only, compared with 1.32 with standard error 0.19 for direct plus proxy data. Presumably, these techniques would extract more useful information from the proxy data in other settings where the proxy data are more tightly correlated with the direct data.

Another potential limitation is the difficulty of accurately recalling food intake and the possibility of misclassification of consumption level. However, because we were assessing intake in the recent past right before the economic and political change in 1989 (subjects were interviewed in the mid-1990s on usual diet before 1990), the recall should be enhanced by the sharp distinction in the general availability of foods at that time. Because the dietary hypotheses being examined in this study were not well known among Polish residents, any recall bias would tend to be random; hence, the ORs would tend to be biased toward the null value. The chance for misdiagnosis of cancer is slight, because 90.2% of cases were histologically confirmed, with the remainder being diagnosed by exploratory surgery.

In summary, our data suggest that diets rich in grains (carbohydrates) and low in fruits and dark green-yellow vegetables (α- and β-carotenes and fiber from fruits and vegetables) may increase the risk of stomach cancer. Such a typical Polish diet prior to 1990 may have contributed to the high incidence of stomach cancer in that country.

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Appendix A
Individual Foods Included in Each Food Group

Food Group	Individual Foods
Fruits and fruit juices	Apples, apple compote, applesauce; bananas; peaches, apricots in season; pears, pear compote; plums, plum compote; watermelon in season; strawberries in season; oranges, tangerines; orange juice, grapefruit juice; other fruits; other juices; prunes, raisins; rhubarb in season; pierogi/pancake w/fruits
Fruits	Excludes orange juice, grapefruit juice, other juices from "Fruits and fruit juices" group
Vegetables	Green beans; peas; dried beans; pea or bean soup; corn; red beets; red beet soup; summer squash; tomato juice; raw tomatoes; sauerkraut not cooked; cauliflower, brussels sprouts; pumpkin excl. marinated; cooked spinach; cooked cabbage or sauerkraut; coleslaw, raw cabbage; cooked carrots, mixed vegetables w/carrots; raw carrots; lettuce (Boston type); french fries, fried potatoes; potato pancakes; other potatoes; vegetable soup; salted sour cucumbers; zucchini; green pepper; radishes; raw celeriac; mushrooms; pierogi/pancake w/cabbage
Cruciferous	Sauerkraut not cooked; coleslaw, raw cabbage; cooked sauerkraut, cooked cabbage; cauliflower, brussels sprouts; cooked spinach; radishes; pierogi/pancake w/cabbage
Tubers, roots	Cooked carrots, mixed vegetables w/carrots; raw carrots; red beets; red beet soup; raw celeriac; french fries, fried potatoes; potato pancakes; other potatoes
Allium	Chives, green onion; leeks; yellow onion; garlic
Raw vegetables	Raw tomatoes; coleslaw, raw cabbage; lettuce (Boston type); green pepper; radishes; raw carrots; raw celeriac
Pickled/Salted vegetables	Tomato juice; sauerkraut; salted sour cucumbers; other pickled/marinated vegetables
Dark green/yellow vegetables	Pumpkin excl. marinated; cooked spinach; cooked carrots, mixed vegetables w/carrots; raw carrots
Grains	Rice; spaghetti; other pasta; pizza; white rolls, french bread; white bread; dark bread; sweet bread/rolls; cookies and doughnuts; corn flakes; hot cooked cereal soup; cooked groats; pierogi/pancake w/meat; pierogi/pancake w/farmer cheese; pierogi/pancake w/cabbage; pierogi/pancake w/fruit; noodle/groats soups; other noodles; corn
Bread, cereal, rice, & pasta	Excludes corn; noodle/groats soups from "Grains" group
Whole grains	Cooked groats; hot cooked cereal soup; dark bread
Refined grains	Excludes "Whole grains" group from "Bread, cereal, rice, & pasta" group and includes sugar; layer cake; crisp biscuits-shortbread
Dairy products	Butter; cold cereal soup; hot cereal soup; yogurt; kefir or sour milk; buttermilk; whole milk; 2% milk; milk in coffee/tea; cream; sour cream; moldy cheese; spread cheese; homogenized cheese; farmer cheese; hard cheese; ice cream; cream-salad dressing; pierogi/pancake w/farmer cheese
Meat, poultry, and fish	Smoked ham; processed smoked meats; bacon; sausages; hot dogs; pork meat loaf; pork chops; pork roast; roast beef; beef stew, pot pie; steak tartar; fried beef steak, hamburger; smoked poultry; other chicken; duck or goose; fried fish; broiled/baked fish; smoked fish; liver; liverwurst; pierogi/pancake w/meat; spaghetti w/meat
Poultry	Includes only poultry from "Meat, poultry, and fish" group
Fish	Includes only fish from "Meat, poultry, and fish" group
Red meat	Excludes "Poultry, fish" group from "Meat, poultry, and fish" group
Smoked meat/fish	Smoked ham; processed smoked meats; smoked poultry; smoked fish
Sausage	Sausage; hot dog
Sweets	Sugar; ice cream; other cookies or doughnuts; sweet breads/rolls; layer cake; chocolate; non-chocolate candy; crisp biscuits-shortbread; cakes, cheesecake; poppy-seed cake; soft drinks; pierogi/pancake w/fruits

Appendix B
Cutpoints for Quartiles of Food Group (Frequency per Week)

Food Group	Quartiles Q1 (low)	Q2	Q3	Q4(high)
Fruits (included juices)	<2.1	2.1–4.8	4.9–7.0	>7.0
Fruits (excluding juices)	<2.2	2.2–4.1	4.2–7.0	>7.0
Vegetables	<16.8	16.8–20.9	21.0–26.6	>26.6
Cruciferous	<2.8	2.8–4.1	4.2–6.3	>6.3
Tubers, roots	<7.7	7.7–9.7	9.8–11.9	>11.9
Allium	<1.9	1.9–3.4	3.5–6.2	>6.2
Raw	<3.5	3.5–4.8	4.9–7.7	>7.7
Pickled, salted	<1.4	1.4–2.7	2.8–4.2	>4.2
Dark green-dark yellow vegetables	<0.7	0.7–1.3	1.4–2.8	>2.8
Raw fruits, vegetables	<5.6	5.6–9.7	9.8–14.0	>14.0
Grains	<19.6	19.6–23.5	23.6–27.5	>27.5
Bread, cereals, rice, pasta	<17.5	17.5–21.2	21.3–25.2	>25.2
Whole grains	<1.0	1.0–2.6	2.7–4.7	>4.7
Refined grains	<15.4	15.4–25.2	20.3–25.2	>25.2
Dairy products	<18.9	18.9–25.8	25.9–32.9	>32.9
Meat, poultry, and fish	<10.1	10.1–13.5	13.6–17.1	>17.1
Poultry	<0.7	≥0.7		
Fish	<0.7	0.7–1.3	1.4–2.1	>2.1
Red meat	<8.0	8.0–11.1	11.2–14.5	>14.5
Smoked meat/fish	<1.4	1.4–2.1	2.1–2.8	>2.8
Sausages	<2.1	2.1–3.4	3.5–4.9	>4.9
Fats, oils, sweets	<21.2	21.2–27.8	27.9–34.8	>34.8
Sweets	<16.8	16.8–24.4	24.5–32.9	>32.9

Appendix C
Cutpoints for Quartiles of Nutrient Intake per Week (Density Variables)

Nutrient	Quartiles Q1 (low)	Q2	Q3	Q4 (high)
Calories[a] (kcal)				
Males	<2555.9	2555.9–3035.7	3035.8–3617.7	>3617.7
Females	<1954.4	1954.4–2314.4	2314.5–2671.5	> 2671.5
Protein (g)	<34.9	34.9–37.4	37.5–40.4	>40.4
Fat (g)	<39.1	39.1–42.4	42.5–45.1	>45.1
Saturated fat (g)	<14.0	14.0–15.7	15.8–17.0	>17.0
Carbohydrates (g)	<111.1	111.1–118.9	119.0–127.0	>127.0
Cholesterol (mg)	<144.6	144.6–167.9	168.0–196.1	>196.1
Sodium from foods (mg)	<2065.4	2065.4–2216.3	2216.4–2377.2	>2377.2
Fiber (g)	<6.1	6.1–6.7	6.8–7.5	>7.5
from fruits & vegetables (g)	<2.6	2.6–3.2	3.3–4.1	>4.1
from beans (g)	<0.4	0.4–0.6	0.61–1.00	>1.00
Vitamin C (mg)	<21.6	21.6–27.1	27.2–34.5	>34.5
Folate (μg)	<99.6	99.6–110.4	110.5–121.0	>121.0
Vitamin E (a-te)	<2.2	2.2–2.6	2.7–3.2	>3.2
Vitamin A (RE)	<660.7	660.7–842.1	842.2–1143.6	>1143.6
Retinol (μg)	<381.8	381.8–577.2	577.3–884.5	>884.5
Carotenoids				
α-carotene (μg)	<492.4	492.4–720.9	721.0–1112.1	>1112.1
β-carotene (μg)	<0.5	0.5–1.3	1.4–3.0	>3.0
lycopene (μg)	<657.5	657.5–1195.3	1195.3–2001.4	>2001.4
lutein (μg)	<382.3	382.3–648.6	648.6–1027.2	>1027.2
cryptoxanthin (μg)	<229.3	229.3–349.9	350.0–516.2	>516.2

a: Calorie intake is not density variable.

Appendix D
Evaluating of the Value of Incorporating Proxy Data in the Analyses

The following methods were used to assess estimates of ORs and their standard errors with the use of the proxy data as well as direct exposure measurements in cases. The key assumption is that direct exposure measurement is the "gold standard" so that, conditional on the direct measurement, the proxy measurement is not predictive of disease risk. We also assume that direct measurements are missing at random among cases. The analysis uses proxy data to estimate the missing direct measurement. If the proxy and direct data are poorly correlated, the analysis implicitly puts less weight on cases with proxy data than on cases with direct data.

First, consider male cases and controls only. Let n_{ijc} be the number of cases with true (X) and proxy (W) measurements at level i (i = 1,2) of X and at level j (j = 1,2) of W. Let n_{jw} be the number of cases with only proxy measurements at level j of W. Let n_{ix} be the number of cases with only true measurements at level i of X. Let m_{ix} be the number of controls at level i of X. We assume all controls provided true data and no proxy data. Finally, let p_{ij} be the true proportions of cases at levels i of X and j of W satisfying $\Sigma_{ij}\, p_{ij} = 1$. Assuming that direct measurements are missing at random among cases, we estimate p_{ij} from the cases by maximizing the log-likelihood

$$P = n_{11c}\ln(p_{11}) + n_{12c}\ln(p_{12}) + n_{21c}\ln(p_{21}) + n_{22c}\ln(1-p_{11}-p_{12}-p_{21}) + n_{1w}\ln(p_{11}+p_{21}) + n_{2w}\ln(1-p_{11}-p_{21}) + n_{1x}\ln(p_{11}+p_{12}) + n_{2x}\ln(1-p_{11}-p_{12}).$$

In this expression, data, n_{jw}, from cases who have proxy information but no direct measurements, give some information on the true exposure level because, for example, $(p_{11} + p_{21})$ is the probability that the proxy measurement is at level 1, obtained by summing over the unknown direct measurement. The covariance matrix of the quantities $\hat{p}_{11}$, $\hat{p}_{12}$, and $\hat{p}_{21}$ that maximize the log-likelihood are estimated from the observed value of the inverse of minus the second cross-derivative of P, evaluated at $\{\hat{p}_{ij}\}$.

The logarithm of the odds ratio (OR) = OR(D,X) is estimated as

$$\hat{\eta} = \ln\{(\hat{p}_{11} + \hat{p}_{12})/(1 - \hat{p}_{11} - \hat{p}_{12})\} - \ln(m_{1x}/m_{2x}).$$

The variance of $\hat{\eta}$ is estimated from the delta method by differentiation with respect to p_{11}, p_{12}, and m_{ix}, and by noting that m_{2x} = number of controls – m_{1x}, that $\hat{p}_{11}$ and $\hat{p}_{12}$ are independent of m_{ix}, and that we can estimate $\mathrm{Cov}(\hat{p}_{11}, \hat{p}_{12})$ as described previously.

The variance of $\hat{OR}$ is estimated as $(\hat{OR})^2\, \hat{Var}(\hat{\eta})$.

These procedures thus yield estimates $\hat{OR}$ and $\hat{Var}(\hat{OR})$ separately for men and for women. To obtain a summary estimate of ln(OR), we take a weighted average of the gender-specific estimates, $\{\hat{\eta}\,\text{male}/\hat{Var}(\hat{\eta}\,\text{male}) + (\hat{\eta}\,\text{female})/\hat{Var}(\hat{\eta}\,\text{female})\}V$, where $V = \{1/\hat{Var}(\hat{\eta}\,\text{male}) + 1/\hat{Var}(\hat{\eta}\,\text{female})\}^{-1}$ is the estimated variance of the estimated summary ln(OR). The estimated summary OR is obtained by exponentiation and has estimated variance $(\hat{OR})^2 V$.